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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,727	09/14/2005	Martin Krause	BB-124	1308
23557	7590	04/01/2008	EXAMINER	
SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950			MEAH, MOHAMMAD Y	
			ART UNIT	PAPER NUMBER
			1652	
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			04/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,727	KRAUSE ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 01 January 2008.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 9-21 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-8 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Claims 1-8 are pending. Claims 1-8 were examined in the previous action. With supplemental amendment of this application, the applicant, on dates 1/1/08, amended claims 1 and 6 are for further examination. Claims 9-21 remain withdrawn.

Claim Rejections

35 U.S.C 11235 U.S.C 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in that to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of identification and quantification of a genus of peptide using a genus of reagent comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb and Zn metals chelated to any chelating agents and any chemical compound bound to

solid support and use of any enzyme to cleave the peptide from protein or solid support then using any HPLC/MS methodology. The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of proteins or chelating agents, chemical coupling reagent and enzyme used in cleavage. Since extent of bounding and selectivity of metal depend on the nature of chelate, linker group and cleavage depends on the nature of enzyme and their respective physical and chemical characteristics given this lack of description of representative protein, chelate, enzyme species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants argument against 112 written description rejection, described on their amendment page 8, is considered but not found persuasive because although the specification teaches method of identification and /or quantification of specific protein using few specific chelating agents such as, DOTA macrocycle, specific metals such as from lanthanides, specific functional group such as biotin type linker group, specific cleaving enzyme such as a trypsin, pepsin etc, does not teach methods of identification and quantification of a genus of peptide using a genus of reagent comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb and Zn metals chelated to any chelating agents and any chemical compound bound to solid support and to peptide and use of any enzyme to cleave the peptide from protein or solid support then using any HPLC/MS methodology. Complexation of known metal to known multidenate chelate is well known, so is the specificity of specific protease to hydrolyse peptide bond. Moreover binding of

polypeptide to a chemical binding agent depends on the nature of functional group of the binding agent. All those metal described in the instant claims would not form metal chelate to **any chelating agent** described in the claims, nor does any **enzyme cleaves any peptide bond**. Moreover metal binding to a chelating agent, binding of polypeptide to chemical functional group needs a sufficient structural knowledge of the chelating agent and chemical functional group. However as explained above, methods of identification and quantification of a genus of peptide using any of Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, .Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La,, Li, Lu, Mn, Na, Nd. Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb or Zn metals chelated to any chelating agents and any chemical compound bound to solid support and use of any enzyme to cleave the peptide from solid support then using any HPLC/MS methodology using a genera of chelating agents, chemical functional group and cleaving enzyme, recited in the claims is a large variable genus that applicant do not teach how all these diverse genera of chelating agents, chemical functional group and cleaving enzyme will have recited function or do not teach sufficient structure to provide the recited function to their structure. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identification/and or quantification of specific protein comprising using macrocyclic lanthanides chelate complex comprising DOTA macrocycle, biotin type linker group, and a protease as cleaving enzyme not reasonably provide enablement for methods of identification and quantification of a genus of peptide using a genus of reagent comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, .Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La,, Li, Lu, Mn, Na, Nd. Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb and Zn metal chelate complex comprising any chelating agents and any chemical compound bound to solid support and use of any enzyme to cleave the peptide from protein or solid support then using any HPLC/MS methodology. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-8 are so broad as to encompass methods of identification and quantification of a genus of protein using a genus of reagent comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, .Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La,, Li, Lu, Mn, Na, Nd. Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb or Zn chelate complex comprising any chelating agents and any chemical compound bound to solid support and use of any enzyme to cleave the peptide from protein or solid support then using any HPLC/MS methodology. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins, as well as broad class of reagents used comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, .Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La,, Li, Lu, Mn, Na, Nd. Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb and Zn chelate complex comprising any chelating agents and any chemical compound bound to solid support and use of any enzyme to cleave the peptide from protein or solid support then using any HPLC/MS

methodology, broadly encompassed by the methods of the claims. The specification fails to describe how any of the said metal chelate selectively bind any protein and/ or peptide and any linker group binds said selected moiety to solid support then any enzyme cleaves the bound moiety from solid support. The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of protein, metal chelate, linker group and cleaving reagent comprising any enzyme as discussed above. As the structure of the claimed substances are not defined in any way, one of ordinary skill in the art would not be able to make and use any such substances without undue experimentation to first find what substances in fact fall within the claimed class. Furthermore, the claimed class of compounds is likely to include many compounds, which one of ordinary skill in the art would be unable to make and use without undue experimentation, even if it was known or expected that the substance be within the scope of the claims.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of identification and quantification of a genus of peptide using a genus of reagent comprising reagent comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, .Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La,, Li, Lu, Mn, Na, Nd. Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb and Zn metal chelate complex comprising any chelating agents and any chemical compound bound to solid support and use of any enzyme to cleave the peptide from protein or solid support then using any HPLC/MS methodology. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of substances having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicants' arguments against rejection of the claims under 35 USC 112 first paragraph enablement requirement are acknowledged but not found persuasive as explained above. Although the specification is enabling for method of identification/and or quantification of specific protein comprising a known protein using macrocyclic lanthanides chelate complex comprising DOTA macrocycle, biotin type linker group, and a trypsin or pepsin etc as cleaving enzyme, does not reasonably provide enablement for methods of identification and quantification of a genus of protein using any of the metal chosen from the group comprising Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb or Zn complexed with these diverse genera of chelating agents and having a genera of chemical functional group bind to a genera of protein and then cleaving by a genera of enzyme. It is well known in the art that binding of polypeptide to a chemical binding agent depends on the nature of functional group of the binding agent. It is well known in the art that chelate formation of a metal to a chelating agent depends on the structure and nature of functional group of the chelating agent. It is well known in the art that all enzyme will not cleave a peptide bond, only specific protease does. All those metal described in the instant claims would not form metal chelate to **any type chelating agent** described in the claims, nor does any **enzyme cleaves peptide bond**. Moreover metal binding to chelating agent, binding of polypeptide to chemical functional group needs the knowledge of sufficient structural knowledge of the chelating agent and chemical

functional group. To find out which chelating agent among these enormous number of chelating agent (having no knowledge of structure or function) molecules that have said chelation activity with the said metal would be required the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue experimentation**. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection of 1-8 under 35 U.S.C. 102(b) as being anticipated by Carr et al. (WO 0047548) is withdrawn after accepting applicant's argument.

However Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Aebersold et al. (WO 00/11208, from IDS)

Claims 1-8 directed to method of identification and quantification of protein in sample using A-Y-PRG reagent wherein metal (any of the following : Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La., Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tin, V, W, Y, Yb or Zn) chelate is Y; A bound to supporting material and PRG bound to protein wherein after selection of the protein it is cleaved from the support by a enzymatic cleavage and then analyze the protein by Mass spectrometry.

Aebersold et al. teach method of identification and quantification of protein in sample using a reagent A-L-PRG, wherein A linked to solid support and covalently linked to L (L may or may not contain reactive group), L -PRG reacts with protein reactive group, wherein linker L comprise a chelating agent such as nitrilotriacetic acid chelated to Ni (page 12) wherein after selection of the protein it is cleaved from the support by a enzymatic cleavage (page 14) and then analyze the protein by Mass spectrometry .

Art Unit: 1652

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Mohammad Meah/
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